Colectomy before the development of malignancy in cases of familial polyposis is an excellent example of cancer prevention. A positive family history of the disease usually confirms its familial nature, but occasional cases when the family history is uncertain present diagnostic problems. Moreover, since the disease is genetically controlled occasional cases may be expected *de novo* as a result of mutation. Diagnostic difficulties arise because of wide variation in the time of onset of clinical manifestations of the disease. B. C. Morson and his colleagues think that this variation may result from the existence of modifying genes. A recent observation of diagnostic value is that the ultrastructure in the polyps and unaffected mucosa differs between familial and non-familial cases.[13]

The list of known carcinogens in the human environment continues to grow. At the Courtauld Institute penicillic acid, penicillin G, and parasorbic acid have been found to be carcinogenic for the subcutaneous tissues of the rat, and workers at the Royal Beatson Memorial Hospital in Glasgow have confirmed the finding of Japanese workers[14] that isoniazid induces lung tumours in mice. At present it is difficult to know whether substances shown to be carcinogenic in animals necessarily constitute cancer hazards in man. In the case of carcinogens which produce their effects indirectly through metabolites it is important to know as much as possible about the metabolic pathways both in man and in animals. In this connexion the discovery of a mechanism for the oxidation of aromatic amines to form carcinogenically active N-hydroxylated compounds[15–17] has opened up a wide new field of inquiry.

A new technique, echo-encephalography, for localizing intracranial lesions by ultra-sound waves has been found of value in detecting displacement of mid-line structures and ventricles, particularly in old and debilitated patients. So far it has not been possible to locate tumours precisely by the sole use of this technique, which was originally developed by Leksell in 1956.[18–20] Physicists have been busy tackling problems in dosimetry posed by new methods for delivering high-energy radiation. Though knowledge of factors which modify the patient's sensitivity to radiation—for example, oxygen tension, temperature, and concentration of sulphydryl groups—is increasing, it has so far led to no dramatic improvement in the results of radiotherapy. In the field of chemotherapy it has been suggested that susceptibility of tumour tissue to alkylating agents is related to the ratio of protein-bound to acid-soluble sulphydryl levels. Radiotherapy as well as chemotherapy may be advanced if current attempts to modify this ratio by inducing *p*H changes and by dyes of the redox type, which take part in oxidation–reduction reactions, meet with success.

In the embryo the mesonephros is derived from primitive mesenchyme. This versatile tissue also counts the adrenal cortex and the gonads among its progeny. It is then perhaps not surprising that the kidney responds to changes in hormone levels, and that the growth of renal tumours is affected by the administration of hormones or by the removal of endocrine glands. In this connexion the researches of H. J. G. Bloom and his colleagues offer a ray of hope for certain cases of advanced renal cancer.

Fundamental to all this work are the many studies on the structure and nature of nucleic acids that are being undertaken. Probably it is from such researches that many of the secrets of the cancers will eventually emerge. Though the workers engaged on these studies are to-day often a long way from the clinical treatment of cancer, it is with them that most of the hope for the future now lies.

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ANTIBIOTIC OTOTOXICITY

It is now an axiom that antibiotic treatment may sometimes do much more harm than good, and this is true particularly of antibiotics capable of damaging the eighth nerve. Most of these belong to the broad group which includes streptomycin, dihydrostreptomycin, neomycin, and kanamycin. The parenteral administration of any of these is unjustified except for a serious purpose and with the possibilities of this toxic effect constantly in mind. The treatment of tuberculosis is one thing; that of a chronic infection of the urinary tract for which there are alternative drugs is quite another. Worse than this, some of the 22 patients with vestibular damage due to streptomycin described by T. Cawthorne and D. Ranger[1] had been given only a few grammes, no doubt in mixtures with penicillin, as cover for operations, among which are mentioned "hernia" and "arthrodesis of toe." Unnecessary prophylaxis of this kind was also responsible for some of the tragic cases of dihydrostreptomycin deafness described by G. E. Shambaugh and colleagues,[2] who protest in the strongest terms against the inclusion of this antibiotic in

proprietary mixtures with names not betraying their contents. Whereas streptomycin attacks particularly the vestibular branch of the nerve and dihydrostreptomycin the auditory, the other antibiotics in this general group, notably neomycin and kanamycin, affect the auditory branch almost exclusively. Deafness so produced is permanent.

The whole subject has recently been reviewed by W. Leach,[3] who lists nine ototoxic antibiotics. The inclusion of polymyxin B is an error, as is the statement that it is "never used parenterally." It is used in this way and damage to the eighth nerve is not a recognized hazard from it. As the author admits, the evidence against ristocetin is slender and doubtful. That leaves the large group already referred to, including framycetin, which in fact has been shown to be neomycin B,[4] and two others, viomycin and vancomycin. The original material in this paper includes accounts of four patients treated at St. Thomas's Hospital with neomycin who suffered loss of hearing. In one there was renal disease, and another was an elderly man who received excessive doses (6 g. on each of six occasions) by instillation into a thoracic empyema. In the remaining two renal function was considered normal, and the dose was not excessive, though treatment—for bacterial endocarditis—was continued in one of them for six weeks. It must unfortunately be recognized that prolonged treatment with neomycin even in moderate doses and in patients with good renal function entails serious risk. Kanamycin, an otherwise very similar antibiotic, is believed to be less ototoxic, though there are plenty of records of loss of hearing from it in predisposed patients. Some encouragement to its use may be found in a case of bacterial endocarditis recorded by L. P. Garrod and Pamela M. Waterworth.[5] This patient received 1 g. of kanamycin daily together with penicillin for six weeks, and recovered with no sign of damage to the eighth nerve. This patient was a woman aged 42; Leach's patient with bacterial endocarditis was a woman aged 45, and she was treated for exactly the same period with neomycin, and with a dose reduced from 1 to 0.5 g. from the tenth day onwards.

It is usual to recommend that during the use of these antibiotics a careful watch should be kept for signs of damage to the eighth nerve. This should of course be done, and administration stopped—unless the patient's life is at stake—when any such signs appear. Unfortunately this is not an adequate safeguard, because a long latent period—sometimes even of several months—may elapse before the effect becomes manifest. The interval may be such that cause and effect are not connected. Thus it is always worth while to inquire of patients with rapid and unexplained loss of hearing whether they have been given any injections in the recent past. In Leach's patients loss of hearing was first complained of 1, 3, 3, and 4 weeks after the treatment had ended, and he offers no evidence that any tests could have detected what was going on at an earlier stage.

There are much more positive ways of guarding against these disasters. The foremost of these is strictly to reserve these antibiotics for clear and serious indications. The second is always to review the possibility of impaired renal function, for even a moderate degree of this reduces the rate of excretion and produces the climbing blood levels which alone can cause damage during short-term treatment. In Cawthorne and Ranger's series of patients with vestibular damage after small total doses of streptomycin were patients with pyelitis in a solitary kidney, tuberculosis in a solitary kidney, and nephrolithiasis. Diabetic nephropathy was doubtless responsible in the case reported by A. Lustberg and M. Hamburger,[6] a 52-year-old man already blind from diabetic retinitis who was rendered also totally deaf by treatment with kanamycin for boils. Lesser degrees of renal impairment than these are also to be feared. Even those almost normally associated with advancing age may delay excretion, and very serious thought should be given to the administration of these antibiotics to any elderly patient. Thirdly, whenever there is the slightest reason to doubt renal efficiency, the antibiotic must be assayed in the blood and the dose regulated accordingly. A. A. C. Dutton and P. C. Elmes[7] found it necessary to do this at frequent intervals to control the dose of vancomycin in uraemic patients, and devised a method for the purpose which took only five hours. A more leisurely test will often serve, but if facilities for any such tests are not available the clinician using an ototoxic antibiotic in a patient with poor renal function is taking a grave responsibility.

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HAEMAGGLUTINATION IN VIRAL HEPATITIS

Since Hirst[1] first discovered that influenza virus can agglutinate avian erythrocytes many other viruses have been found with similar activity. Often the agglutination is brought about by the direct action of the virus on the surface of the erythrocyte, and sera from convalescent patients specifically inhibit such agglutination by means of their antiviral antibodies. Since experimental animals are not susceptible to the virus of infectious hepatitis many

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